IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:		§	
	Ami ARONHEIM et al	§	
Serial No.:	09/777,856	§	
Filed:	February 7, 2001	§	Group Art Unit: 1633
For:	NUCLEIC ACID CONSTRUCT SYSTEM AND METHOD UTILIZING SAME USEFUL FOR IDENTIFYING PROTEIN-PROTEIN INTERACTIONS	§	
		§	Attorney Docket: 01/21605
Examiner:	Maria Marvich	§	

Commissioner for Patents
P. O. Box 1450
Alexandria VA 22313

DECLARATION UNDER 37 CFR §1.131

I, Ami Aronheim, declare as follows:

1. I am a co-inventor of the invention described and claimed in the above-identified U.S. Patent Application declare as follows:

2. I am familiar with the Official action mailed on January 26, 2006, with respect to the above-identified application, in which the Examiner cited Takemaru and Moon, *The Journal of Cell Biology 149(2), April 17, 2000* to reject claims 1-2, 6-8, 27-29 and 33-35 under 35 U.S.C. 102(a).

3. That the publication date, and thus the 35 U.S.C. §102(a) date of the Takemaru and Moon reference is April 17, 2000.

4. That the aforementioned publication of Takemaru and Moon is not prior art to our invention, inasmuch as I and my co-inventors had actually reduced to practice, and thus made our invention, prior to the April 17, 2000 publication date of Takemaru and Moon.

5. In evidence of such reduction to practice, I attach herewith a copy of my four page correspondence dated prior to April 17, 2000 (date blacked out) with the editor of Nature Biotechnology which presents an Abstract of our work describing the

successful reduction to practice of our claimed technology along with its advantages as well as results obtained using same.

6. That the rejection of claims of our invention over Takemaru and Moon should be withdrawn since Takemaru and Moon is not prior art relative to the invention that is the subject of the above-identified patent application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dr. Ami Aronheim

Dated: May 4, 2006

Delivered-To: aronheim@techunix.technion.ac.il
Date: Fri, 24 Mar 2000 09:00:05 -0600
From: harvey bialy <h.bialy@natureny.com>
X-Accept-Language: en
MIME-Version: 1.0
To: aronheim@techunix.technion.ac.il, n.dewitt@natureny.com
Subject: PS-2837

Dear Dr. Aronheim,

Thank you for your inquiry. Based on what you have sent, your manuscript appears quite appropriate for Nature Biotechnology, and we would welcome reading it with the intention of submitting it for peer review. But please understand that until we see the paper itself, we can make no firm commitment to having it formally considered.

When you submit the manuscript please address it to Dr. Natalie DeWitt, Research Editor, and refer to number PS-2837 in your cover letter. Please be sure your paper is in the style outlined in our guide to authors (which can be found on our web site at: http://biotech.nature.com/author/).

Thank you for thinking of Nature Biotechnology as a place to publish your research.

Sincerely yours,

Harvey Bialy, Ph.D.
Editor at Large

biotech wrote:

> -----Original Message-----
> From: aronheim@tx.technion.ac.il [mailto:aronheim@tx.technion.ac.il]
> Sent: Sunday, March 19, 2000 1:51 AM
> To: biotech@natureny.com
> Cc: aronheim@tx.technion.ac.il
> Subject: Re: Author Presubmission Form
>
> This mail originated from the Nature Biotechnology web site Author
> Presubmission Form.
>
> This is a copy of the email sent in your name to the Nature
> Biotechnology Presubmission Desk.
>

> This is for refrence and does not constitute the promise of being
> printed in Nature.
>
> If you have questions, please address them to biotech@natureny.com and
> include this mail for reference.
>
> Name: Dr. Ami Aronheim
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> Institution: Israel Institute of Technology
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> Other Authors:
> Monika Hubsman
>
> Title of submission:
> Reverse Ras Recruitment System for the identification of
> protein-protein interaction with membrane proteins.
>
> Intended format: article
>
> Brief Paragraph:
> The Editor
> Nature Biotechnology
> 345 Park Avenue South
> New York NY 10010-1707
> telephone: 212.726.9335
> facsimile: 212.696.9635
> March 19th 2,000
>
> Dear Editor,.
> We have send, last week, the following presubmission form via
> electronic mail. Since we did not get any response, we wondered whether
> it did reach your office or you did not come to a final decision yet.
> Therefore, we enclose the presubmission information.

harvey bialy,3/24/0 3:00 PM,PS-2837 3

> The manuscript we wish to submit to Nature Biotechnology describes
> the
> development of a novel approach to study protein-protein interaction,
> specifically designed for membrane proteins. This revolutionary
> approach would enable to identify protein binding to membrane
> receptors, ion channels trasnsporters which contain multiple membrane
> spanning domains The approach preserves their structural constrains by
> expressing these proteins in yeast in their natural environment. This
> is unlike the two hybrid system and the Ras recruitment system
> approaches in which protein-protein interaction should occur in yeast
> at either the nucleus or cytoplasm, respectively. We have used this
> approach to identify protein binding to the novel small G protein, Chp,
> in its membrane bound form and identified two clones that exhibit
> specific interaction with the Chp-bait. The biological significance of
> the interaction found following the library screen is yet to be
> determined. However, we feel that the novelty of the approach and the
> biotechnological implications of this method justify the merit for
> publication in a Journal with a wide interest, for investigators from
> multiple research disciplines.
>
> Please let me know if you will be interested in reviewing the full
> length paper.
>
> Ami Aronheim
>
> Fully Referenced Summary Paragraph:
> Reverse Ras Recruitment System for the identification of
> protein-protein interaction with membrane proteins.
>
> Monika Hubsman and Ami Aronheim#
>
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> Rappaport Family Institute for Research in the Medical Sciences and the
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>
> #To whom correspondence should be addressed.
>
> Protein-protein interaction plays a major role in all biological

> processes 1. The currently available genetic methods such as: the two
> hybrid system 2, 3 and the protein recruitment systems 4, 5 are
> relatively limited in their ability to identify interaction with
> integral membrane proteins such as G-protein coupled receptors, hormone
> receptors, cytokine receptors, transporters, ion-channels and membrane
> phospholipids. Here we describe the development of a reverse Ras
> recruitment system approach in which the protein-bait used encodes for
> a membrane protein. The bait is expressed in its natural environment,
> the membrane, whereas, the protein partner (the prey) is fused to
> cytoplasmic Ras mutant. Protein-protein interaction between the protein
> encoded by the prey and the membrane-bait results in Ras membrane
> translocation and activation of a viability pathway in yeast. Since the
> fusion of a random cDNA to Ras may result in translocation of Ras to
>
> the membrane independent of bait interaction, we devised a dual
> inducible expression system for the bait and prey proteins to enable
> rapid selection of transformants in which their growth is attributed
> solely on specific protein-protein interaction between the bait and
> prey proteins. The reverse RRS approach greatly extends the usefulness
> of the protein recruitment systems and the use of integral membrane
> proteins as protein baits. The system serves as an attractive approach
> to explore novel territories of protein-protein interaction with high
> specificity and selectivity where other methods fail to function.
>
> References Cited in Summary:
> References:
>
> 1. Mendelsohn, A.R. & Brent, R. Science 284, 1948-1950 (1999).
> 2. Fields, S. & Song, O.K. Nature 340, 245-246 (1989).
> 3. Colas, P. & Brent, R. Trends Biotechnol 16, 355-63 (1998).
> 4. Aronheim, A., Zandi, E., Hennemann, H., Elledge, S. & Karin, M. Mol.
>
> Cell. Biol. 17, 3094-3102 (1997).
> 5. Broder, Y.C., Katz, S. & Aronheim, A. Curr. Biol. 8, 1121-1124
> (1998).
>
> Other Information:
> Dear Editor,
> Since we did not receive any response to our previous presubmission ,
> we can not exclude the possibility that it did not reach your editorial
> office. Therefore, we would greatly appreciate your response of any
> kind regarding this presubmission.
> Ami Aronheim